From the INTERNATIONAL SEARCHING AUTHORITY

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HUBER & SCHÜSSLER Attn. Schussler, Andrea Truderinger Strasse 246 D-81825 München GERMANY Huber & Patenta 0 9 DE	or the declaration		
	Date of mailing (day/month/year) 08/12/2003		
Applicant's or agent's file reference			
M 4516/st	FOR FURTHER ACTION See paragraphs 1 and 4 below		
International application No. PCT/EP 03/04083	International filing date (day/month/year) 17/04/2003		
Applicant			
MTM LABORATORIES AG			
1. X The applicant is hereby notified that the International Search Report has been established and is transmitted herewith. Filing of amendments and statement under Article 19: The applicant is entitled, if he so wishes, to amend the claims of the International Application (see Rule 46): When? The time limit for filing such amendments is normally 2 months from the date of transmittal of the International Search Report; however, for more details, see the notes on the accompanying sheet. Where? Directly to the International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Fascimile No.: (41-22) 740.14.35 For more detailed instructions, see the notes on the accompanying sheet. 2. The applicant is hereby notified that no International Search Report will be established and that the declaration under Article 17(2)(a) to that effect is transmitted herewith. With regard to the protest against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that: the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.			
no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.			
4. Further action(s): The applicant is reminded of the following: Shortly after 18 months from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in Rules 90bis.1 and 90bis.3, respectively, before the completion of the technical preparations for international publication. Within 19 months from the priority date, a demand for international preliminary examination must be filed if the applicant			
wishes to postpone the entry into the national phase until 30 months from the priority date (in some Offices even later). Within 20 months from the priority date, the applicant must perform the prescribed acts for entry into the national phase before all designated Offices which have not been elected in the demand or in a later election within 19 months from the priority date or could not be elected because they are not bound by Chapter II.			

Name and mailing address of the International Searching Authority European Patent Office, P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016

Authorized officer

Sabine Oblinger

These Notes are intended to give the basic instructions concerning the filing of amendments under article 19. The Notes are based on the requirements of the Patent Cooperation Treaty, the Regulations and the Administrative Instructions under that Treaty. In case of discrepancy between these Notes and those requirements, the latter are applicable. For more detailed information, see also the PCT Applicant's Guide, a publication of WIPO.

In these Notes, "Article", "Rule", and "Section" refer to the provisions of the PCT, the PCT Regulations and the PCT Administrative Instructions, respectively.

INSTRUCTIONS CONCERNING AMENDMENTS UNDER ARTICLE 19

The applicant has, after having received the international search report, one opportunity to amend the claims of the international application. It should however be emphasized that, since all parts of the international application (claims, description and drawings) may be amended during the international preliminary examination procedure, there is usually no need to file amendments of the claims under Article 19 except where, e.g. the applicant wants the latter to be published for the purposes of provisional protection or has another reason for amending the claims before international publication. Furthermore, it should be emphasized that provisional protection is available in some States only.

What parts of the international application may be amended?

Under Article 19, only the claims may be amended.

During the international phase, the claims may also be amended (or further amended) under Article 34 before the International Preliminary Examining Authority. The description and drawings may only be amended under Article 34 before the International Examining Authority.

Upon entry into the national phase, all parts of the international application may be amended under Article 28 or, where applicable, Article 41.

When?

Within 2 months from the date of transmittal of the international search report or 16 months from the priority date, whichever time limit expires later. It should be noted, however, that the amendments will be considered as having been received on time if they are received by the International Bureau after the expiration of the applicable time limit but before the completion of the technical preparations for international publication (Rule 46.1).

Where not to file the amendments?

The amendments may only be filed with the International Bureau and not with the receiving Office or the International Searching Authority (Rule 46.2).

Where a demand for international preliminary examination has been/is filed, see below.

How?

Either by cancelling one or more entire claims, by adding one or more new claims or by amending the text of one or more of the claims as filed.

A replacement sheet must be submitted for each sheet of the claims which, on account of an amendment or amendments, differs from the sheet originally filed.

All the claims appearing on a replacement sheet must be numbered in Arabic numerals. Where a claim is cancelled, no renumbering of the other claims is required. In all cases where claims are renumbered, they must be renumbered consecutively (Administrative Instructions, Section 205(b)).

The amendments must be made in the language in which the international application is to be published.

What documents must/may accompany the amendments?

Letter (Section 205(b)):

The amendments must be submitted with a letter.

The letter will not be published with the international application and the amended claims. It should not be confused with the "Statement under Article 19(1)" (see below, under "Statement under Article 19(1)").

The letter must be in English or French, at the choice of the applicant. However, if the language of the international application is English, the letter must be in English; if the language of the international application is French, the letter must be in French.

The letter must indicate the differences between the claims as filed and the claims as amended. It must, in particular, indicate, in connection with each claim appearing in the international application (it being understood that identical indications concerning several claims may be grouped), whether

- (i) the claim is unchanged;
- (ii) the claim is cancelled;
- (iii) the claim is new:
- (iv) the claim replaces one or more claims as filed;
- (v) the claim is the result of the division of a claim as filed.

The following examples illustrate the manner in which amendments must be explained in the accompanying letter:

- [Where originally there were 48 claims and after amendment of some claims there are 51]:
 "Claims 1 to 29, 31, 32, 34, 35, 37 to 48 replaced by amended claims bearing the same numbers;
 claims 30, 33 and 36 unchanged; new claims 49 to 51 added."
- [Where originally there were 15 claims and after amendment of all claims there are 11]: "Claims 1 to 15 replaced by amended claims 1 to 11."
- [Where originally there were 14 claims and the amendments consist in cancelling some claims and in adding new claims]:
 "Claims 1 to 6 and 14 unchanged; claims 7 to 13 cancelled; new claims 15, 16 and 17 added." or "Claims 7 to 13 cancelled; new claims 15, 16 and 17 added; all other claims unchanged."
- 4. [Where various kinds of amendments are made]: "Claims 1-10 unchanged; claims 11 to 13, 18 and 19 cancelled; claims 14, 15 and 16 replaced by amended claim 14; claim 17 subdivided into amended claims 15, 16 and 17; new claims 20 and 21 added."

"Statement under article 19(1)" (Rule 46.4)

The amendments may be accompanied by a statement explaining the amendments and indicating any impact that such amendments might have on the description and the drawings (which cannot be amended under Article 19(1)).

The statement will be published with the international application and the amended claims.

It must be in the language in which the international application is to be published.

It must be brief, not exceeding 500 words if in English or if translated into English.

It should not be confused with and does not replace the letter indicating the differences between the claims as filed and as amended. It must be filed on a separate sheet and must be identified as such by a heading, preferably by using the words "Statement under Article 19(1)."

It may not contain any disparaging comments on the international search report or the relevance of citations contained in that report. Reference to citations, relevant to a given claim, contained in the international search report may be made only in connection with an amendment of that claim.

Consequence if a demand for international preliminary examination has already been filed

If, at the time of filing any amendments and any accompanying statement, under Article 19, a demand for international preliminary examination has already been submitted, the applicant must preferably, at the time of filing the amendments (and any statement) with the International Bureau, also file with the International Preliminary Examining Authority a copy of such amendments (and of any statement) and, where required, a translation of such amendments for the procedure before that Authority (see Rules 55.3(a) and 62.2, first sentence). For further information, see the Notes to the demand form (PCT/IPEA/401).

Consequence with regard to translation of the international application for entry into the national phase

The applicant's attention is drawn to the fact that, upon entry into the national phase, a translation of the claims as amended under Article 19 may have to be furnished to the designated/elected Offices, instead of, or in addition to, the translation of the claims as filed.

For further details on the requirements of each designated/elected Office, see Volume II of the PCT Applicant's Guide.

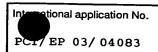


(PCT Article 18 and Rules 43 and 44)

A 4516/at	Applicant's or agent's file reference	FOR FURTHER see Notification of Transmittal of International Search Report		
Applicant MTM_LABORATORIES_AG This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Search Report consists of a total of		ACTION		
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because this figure better characterizes the invention.		_		
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Box I	Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)
This Inte	rnational Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:
1. X	Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:
	Although claims 5-10, 18-29 are directed to a method of treatment of the human body, the search has been carried out and based on the alleged effects of the compound/composition.
2.	Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
з. [Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).
Box II	Observations where unity of invention is lacking (Continuation of item 2 of first sheet)
This Inte	ernational Searching Authority found multiple inventions in this international application, as follows:
	see additional sheet
1.	As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2.	As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3.	As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. X	No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.: 1-19, 22-36, 39-42 (all partially)
Remark	The additional search fees were accompanied by the applicant's protest. No protest accompanied the payment of additional search fees.





Box III TEXT OF THE ABSTRACT (Continuation of item 5 of the first sheet)

The present invention relates to neopeptides and methods useful for the detection and treatment of disorders associated with frameshift mutations in coding microsatellite regions. The neopeptides and methods are applicable in cancers, especially of DNA mismatch repair deficient (MMR) sporadic tumours and HNPCC associated tumours. The neopeptides disclosed in the invention are useful for detection of disorders and in therapy such as e.g. immuno-therapy. The diagnostic methods relate to diagnosis and prognostic assessment of disorders associated with frameshift polypeptides originating from frameshift mutations in coding microsatellite regions of genes based on the detection of immunological entities directed against said frameshift polypeptides in body fluids. With respect to the treatment of cancer, especially of DNA mismatch repair deficient (MMR) sporadic tumours and HNPCC associated tumours, the invention pertains to methods which use immuno therapy with combinatorial mixtures of tumour specific frameshift peptides to elicit a cytotoxic T-cell response specifically directed against tumour cells for use in prevention as well as in curative treatment of cancers and precancers.

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 1-19, 22-36, 39-42 partially

a polynucleotide with the insertion or deletion of one or two A in the All repeat of the gene TAF1B, a polypeptide encoded by said polynucleotide, a method of treatment or detection involving them and a pharmaceutical composition or a diagnostic kit comprising them

2. Claims: 1-19, 22-36, 39-42 partially

a polynucleotide with the insertion or deletion of one or two A in the All repeat of the gene MACS, a polypeptide encoded by said polynucleotide, a method of treatment or detection involving them and a pharmaceutical composition or a diagnostic kit comprising them

3. Claims: 1-17 partially

a polynucleotide with the insertion or deletion of one or two A in the A10 repeat of the gene UVRAG, a polypeptide encoded by said polynucleotide, a method of treatment or detection involving them and a pharmaceutical composition or a diagnostic kit comprising them.

4. Claims: 1-17 partially

a polynucleotide with the insertion or deletion of one or two G in the G9 repeat of the gene ELAVL3, a polypeptide encoded by said polynucleotide, a method of treatment or detection involving them and a pharmaceutical composition or a diagnostic kit comprising them.

5. Claims: 1-17 partially

a polynucleotide with the insertion or deletion of one or two A in the A10 repeat of the gene TCF6L1, a polypeptide encoded by said polynucleotide, a method of treatment or detection involving them and a pharmaceutical composition or a diagnostic kit comprising them.

6. Claims: 1-19, 22, 25-36, 39-42 partially

a polynucleotide with the insertion or deletion of one or two A in the AlO repeat of the gene ABCF1, a polypeptide encoded by said polynucleotide, a method of treatment or detection involving them and a pharmaceutical composition or a diagnostic kit comprising them.

7. Claims: 1-19, 22, 24-36, 39-42 partially

a polynucleotide with the insertion or deletion of one or two A in the AlO repeat of the gene AIM2, a polypeptide encoded by said polynucleotide, a method of treatment or detection involving them and a pharmaceutical composition or a diagnostic kit comprising them.

8. Claims: 1-17 partially

a polynucleotide with the insertion or deletion of one or two A in the AlO repeat of the gene CHD2, a polypeptide encoded by said polynucleotide, a method of treatment or detection involving them and a pharmaceutical composition or a diagnostic kit comprising them.

9. Claims: 1-17 partially

a polynucleotide with the insertion or deletion of one or two A in the All repeat of the gene FLJ11053, a polypeptide encoded by said polynucleotide, a method of treatment or detection involving them and a pharmaceutical composition or a diagnostic kit comprising them.

10. Claims: 1-17 partially

a polynucleotide with the insertion or deletion of one or two A in the All repeat of the gene KIAA1052, a polypeptide encoded by said polynucleotide, a method of treatment or detection involving them and a pharmaceutical composition or a diagnostic kit comprising them.

11. Claims: 1-17 partially

a polynucleotide with the insertion or deletion of one or two A in the A8 repeat of the gene ACVR2, a polypeptide encoded by said polynucleotide, a method of treatment or detection involving them and a pharmaceutical composition or a diagnostic kit comprising them.

12. Claims: 1-19, 23-31 partially

a polynucleotide with the insertion or deletion of one or two A in the All repeat of the gene HT001, a polypeptide encoded by said polynucleotide, a method of treatment or detection involving them and a pharmaceutical composition or a diagnostic kit comprising them.

13. Claims: 3-19, 22-36, 39-42 partially

a frameshift polypeptide U79260, a method of treatment or detection involving it and a pharmaceutical composition or a diagnostic kit comprising it.

14. Claims: 3-19, 22, 23, 25-36, 39-42 partially

a frameshift polypeptide PTHL3, a method of treatment or detection involving it and a pharmaceutical composition or a diagnostic kit comprising it.

15. Claims: 3-19, 23-36, 40-42 partially and 20, 37 completely

a frameshift polypeptide TGFbRII, a method of treatment or detection involving it and a pharmaceutical composition or a diagnostic kit comprising it.

16. Claims: 3-19, 22, 23, 25-36, 39-42 partially

a frameshift polypeptide TCF4, a method of treatment or detection involving it and a pharmaceutical composition or a diagnostic kit comprising it.

17. Claims: 3-19, 22-36, 39-42 partially

a frameshift polypeptide AC1, a method of treatment or detection involving it and a pharmaceutical composition or a diagnostic kit comprising it.

18. Claims: 3-19, 22, 23, 25-36, 39-42 partially

a frameshift polypeptide Sec63, a method of treatment or detection involving it and a pharmaceutical composition or a diagnostic kit comprising it.

19. Claims: 3-19, 22-36, 39-42 partially

a frameshift polypeptide CASP5, a method of treatment or detection involving it and a pharmaceutical composition or a diagnostic kit comprising it.

20. Claims: 3-17 partially

a frameshift polypeptide USLC23A1, a method of treatment or detection involving it and a pharmaceutical composition or a diagnostic kit comprising it.

21. Claims: 3-17 partially

a frameshift polypeptide HSPC259, a method of treatment or detection involving it and a pharmaceutical composition or a diagnostic kit comprising it.

22. Claims: 3-19, 25-36, 40-42 partially and 21, 38 completely

a frameshift polypeptide BAX, a method of treatment or detection involving it and a pharmaceutical composition or a diagnostic kit comprising it.

23. Claims: 3-17 partially

a frameshift polypeptide FTL3L, a method of treatment or detection involving it and a pharmaceutical composition or a diagnostic kit comprising it.

24. Claims: 3-19, 24-31 partially

a frameshift polypeptide OGT, a method of treatment or detection involving it and a pharmaceutical composition or a diagnostic kit comprising it.

25. Claims: 3-17 partially

a frameshift polypeptide MAC30X, a method of treatment or detection involving it and a pharmaceutical composition or a diagnostic kit comprising it.

26. Claims: 3-17 partially

a frameshift polypeptide SLC4A3, a method of treatment or detection involving it and a pharmaceutical composition or a diagnostic kit comprising it.

27. Claims: 3-17 partially

a frameshift polypeptide PRKDC, a method of treatment or detection involving it and a pharmaceutical composition or a diagnostic kit comprising it.

28. Claims: 3-19, 24-31 partially

a frameshift polypeptide MSH3, a method of treatment or detection involving it and a pharmaceutical composition or a

diagnostic kit comprising it.

29. Claims: 18, 19, 22-36, 39-42 partially

a frameshift polypeptide IGFIIR, a method of treatment or detection involving it and a pharmaceutical composition or a diagnostic kit comprising it.

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a. classification of subject matter IPC 7 C07K14/82 G01N33/48

A61K48/00

A61K38/00

C12Q1/68

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 CO7K GO1N A61K C12Q

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, BIOSIS, MEDLINE, EMBASE, SEQUENCE SEARCH, CHEM ABS Data

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DATABASE EMBL 'Online! EST, 10 September 2001 (2001-09-10) NATIONAL INSTITUTES OF HEALTH: "60233245139F1 NIH_MGC_96 Homo sapiens cDNA clone IMAGE:5287496 5', mRNA sequence" Database accession no. BI603282 XP002226919 abstract	1
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Y Further documents are listed in the continuation of box C.	Patent family members are listed in annex.	
Special categories of cited documents: "A" document defining the general state of the art which is not considered to be of particular relevance "E" earlier document but published on or after the international filing date "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "O" document referring to an oral disclosure, use, exhibition or other means "P" document published prior to the international filing date but later than the priority date claimed	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art. "8" document member of the same patent family	
Date of the actual completion of the international search	Date of mailing of the international search report	
4 September 2003	0 8, 12. 03	
Name and mailing address of the ISA	Authorized officer .	
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31–70) 340–2040, Tx. 31 651 epo nl, Fax: (+31–70) 340–3016	Guarinos Viñals, E	

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International	Application No
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	ustion) DOCUMENTS CONSIDERED TO BE RELEVANT	
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
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X	WO 02 04664 A (KNEBEL DOEBERITZ VON MAGNUS; LINNEBACHER MICHAEL (DE); BORK PEER () 17 January 2002 (2002-01-17) examples 1-8 page 6, last paragraph page 7, paragraph 2	1-19, 22-36, 39-42
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C.(Continu	ation) DOCUMENTS CONSIDERED TO BE RELEVANT	PUT	
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A	DI PIETRO C ET AL: "Genomic localization of the human genes TAF1A, TAF1B and TAF1C, encoding TAF148, TAF163 and TAF1110 subunits of class I general transcription initiation factor SL1." CYTOGENETICS AND CELL GENETICS, vol. 89, no. 1-2, 2000, pages 133-136, XP009003813 ISSN: 0301-0171		
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